IN THE **UNITED STATES** PATENT AND TRADEMARK **OFFICE**

Application Number	09/759,345	
Filing Date	January 16, 2001	
First Named Inventor	Douglas H. ROBINSON	
Group Art Unit	1645	
Examiner Name	Robert Zeman	
Attorney Docket Number	2149-107	

Title of the Invention:

AUG 0 1 2003

METHODS FOR THE ISOLATION OF BACTERIA CONTAINING FUKARYOTIC GENES

APPELLANT'S BRIEF

Applicant appeals from the Final Rejection of the claims of the above-referenced patent application dated September 23, 2002. The fee required by 37 C.F.R. §1.17(c), a petition pursuant to 37 C.F.R. §1.116(a) and the fee required for a four month extension of time accompany this brief. The Commissioner is authorized to charge any underpayment or credit any overpayment to deposit account No. 02-2135. The current claims of this application are reproduced in Appendix A.

I. REAL PARTY IN INTEREST

The named inventor is the real party in interest in this appeal.

II. RELATED APPEALS AND INTERFERENCES

Applicants are unaware of any appeals or interferences related to the subject matter of this appeal.

III. STATUS OF CLAIMS

Claims 1-29 are currently pending and are under final rejection as a result of the lice Action mailed Control of the lice Action mailed Contro Claims 1-29 are currently periods.

Office Action mailed September 23, 2002 (Paper 8). Claims 1-29 are appealed.

The following amendments to the claims are filed concurrently herewith:

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- 3. The method according to claim 2 which further comprises subjecting the cells to an a final aerobic culturing step.
 - 26. A cell according to claim 24 that is a bacteria bacterium.
 - 28. A cell according to claim 25 that is a bacteria bacterium.

These amendments have not been entered.

V. SUMMARY OF THE INVENTION

The present invention relates to methods for producing a bacterium that contains a eukaryotic and/or viral gene, which comprises culturing virally-infected eukaryotic cells under low oxygen conditions to produce a bacterium containing a eukaryotic and/or viral gene. Under a preferred embodiment of the invention, the method comprises the steps of (a) culturing virally-infected eukaryotic cells under anaerobic conditions with at least one exposure to aerobic or microaerophilic conditions, (b) culturing cells from step (a) under aerobic conditions, and (c) isolating at least one bacterium that contains a eukaryotic or viral gene. The invention also relates to cells produced by the claimed methods.

The unusual feature of the claimed invention is that by utilizing the methods thereof, it is possible to produce, from a culture of eukaryotic cells, altered cells that have all the morphological characteristics of bacteria (i.e., would be classified as "bacteria" by the objective observer), yet contain one or more eukaryotic or viral genes in their genome without introducing the genes into a bacterial culture by traditional molecular biological techniques. While not wishing to be bound by theory, it appears that the methods of this invention result in "de novo speciation" or "de-evolution" of the eukaryotic cells into bacterial forms. By the exercise of scrupulous attention to sterility, and the use of

multiple controls in the methods, it has been confirmed that the bacteria produced are not the product of contamination at any point in the process and so are not the result merely of contaminating bacteria overgrowing the starting eukaryotic cell culture.

The method is useful for producing bacteria that contain and express a variety of eukaryotic and/or viral proteins. Such cells can be used in fermentation culture to produce these proteins in quantity for use as medicines, diagnositic agents, etc., or can be used to produce vaccines, as well as for any number of other purposes for which traditionally-produced transgenic bacteria are used.

VI. ISSUES

A first issue is whether or not the subject matter of claims 1-29 meets utility requirements of 35 U.S.C. § 101. The Patent Office maintains that because the claims are drawn to a method for "producing" a bacterium, the claims call for the "creation" of a new species and/or "creation of a life form," and are hence based on an incredible utility and are inoperative. Applicant argues that a) the claims are not directed to the "creation of a new life form" or "spontaneous generation of a life form," but rather to de novo speciation of a bacterial cell from a culture of eukaryotic cells and b) regardless of possible doubts, the Applicant has shown through data presented in the specification and in an independent reproduction of the work, that the method does, in fact, function and therefor is demonstrably operative.

A second issue is whether or not a deposit has been made in accordance with the Budapest Treaty. The Patent Office asserts that compliance with the requirements of 35 U.S.C. §112, first paragraph requires that a deposit of micro-organisms be made under the Budapest Treaty. Applicant argues that such deposits have, in fact, been

made, as is stated in the presumptively accurate disclosure of the specification, and as was repeated in the last response prior to issuance of the final Office Action. Applicant is prepared to submit copies of certificates of deposits made by the applicant and again declare that the provisions of the Budapest Treaty have been met, if the veracity of statements in the specification is doubted.

A third issue is whether or not claims 1-29 are enabled by the specification as required by 35 U.S.C. §112, first paragraph. The Patent Office asserts that the specification is enabled for *isolating* a bacterium, it does not reasonably provide enablement for *producing* a bacterium, or for producing any an all bacteriia. Applicant argues a) that the examples of the application show that the methods in fact do function to produce a bacterium as claimed, and further that independent reproduction of the experiments described in the specification confirms that the specification is enabling, and 2) that the specification need not enable production of "any and all" bacteria in order to fulfill the requirements of §112, first paragraph.

A fourth issue is whether or not claims 1-29 meet the definateness requirement of 35 U.S.C. §112, second paragraph. The Patent Office asserts that the claim term "low oxygen conditions" is indefinite, and the recitation of culture steps under "low oxygen conditions" and under "anaerobic conditions" within the same claim is contradictory and confusing. Applicant argues that the term is specifically and clearly defined in the specification in a manner consistent with its accepted meaning in the art, and is therefore definite, and that the recitation of two different culture conditions for two different steps in a multi-step process does not render the claim contradictory or confusing. The Patent Office also asserts that the claims fail to set forth the subject

matter which the applicant regards as his invention, asserting a lack of correspondence in scope between the claims and the way in which the applicant has characterized the invention in its arguments before the Patent Office. The applicant argues that there is no inconsistency between the claims and any characterization of the invention made the the applicant, either in the specification or in subsequent argument. The Patent Office asserts that the use of the terms "derived," "evolved," "pleiomorphic" and "morphology that is neither eukaryotic nor prokaryotic" render the claims indefinite. The applicant argues that these claims have well-established meanings in the art and/or are expressly defined in the specification, and thus would be understood by a person having ordinary skill in the art, and are as definite as the subject matter permits.

A fifth issue is whether or not claims 24-29 meet the written description requirement of 35 U.S.C. §112, second paragraph. The Patent Office asserts that the claim limitation that the claimed cell is not a transgenic cell is not supported by a written description in the specification. Applicant argues that the Patent Office is applying an improper *in haec verba* test, and that a person of ordinary skill in the art would have understood that what was being described and claimed was a cell that was not a transgenic cell.

VII. GROUPING OF THE CLAIMS

Claims 1-29 are grouped together with regard to the issues of utility, enablement and indefiniteness based on alleged lack of correspondence in scope between the claims and the specification.

Claims 1-23, 26 and 28 are grouped separately from claims 24, 25, 27 and 29 with regard to the issues of written description and indefiniteness based on the use of the

allegedly vague claim terms "derived," "evolved" "pleiomorphic" and "morphology that is neither prokaryotic nor eukaryotic."

VIII. ARGUMENT

A. Issues raised in the Office Action about which there is no real dispute

The Office Action raises two issues about which there is no real dispute. First, the examiner has maintained a non-statutory double patenting rejection on the claims as obvious over claims 1-14 of commonly-owned U.S. Patent No. 6,022,730. Paper 8, pages 3-4. Applicant has indicated that an appropriate terminal disclaimer while be filed if any claims subject to this rejection are held allowable. Second, the examiner has objected to claims 26 and 28 due to an informality in the claim language. Paper 8, page 13. This informality has been corrected by an amendment filed concurrently herewith.

B. Rejection under 35 U.S.C. § 101

The examiner has maintained the rejection of all claims under § 101 because "the claimed invention is not supported by either a credible asserted utility or a well established utility, as the disclosed invention is inoperative." Paper 8, page 4. The examiner focuses on the use of the claim term "producing," and maintains that this is synonymous with spontaneous generation of life. Paper 8, pages 5-6. This position is based entirely on semantics and is not reasonably based on either the written description or the positions taken by the applicant during this prosecution.

Contrary to the examiner's assertion, the specification shows by provision of detailed protocols and actual data, that the claimed invention is operative.

Furthermore, the applicant has submitted a detailed report, accompanied by

declarations, that demonstrates through independent corraboration of the results reported in the specification, that the claimed methods do indeed work. What the applicant has invented is a method that allows one to take cultured retrovirally-infected eukaryotic cells, uncontaminated with bacteria, subject them to a series of specific culturing conditions, and obtain at the end a culture of what, from a morphological point of view, can only be described as "bacteria," which contain intact eukaryotic and/or viral genes. The claims express and describe, within the limits of the English language, these methods. With reference to the written description, a person having ordinary skill in the art would clearly understand that the applicant is not claiming "spontaneous generation" of life (i.e., the creation of life from lifeless matter), but rather a process that results in the alteration of a living life form. Conceptually, this is no different from what is achieved by such techniques as DNA transformation of a plant cell to express one or more bacterial cells, creation of a transgenic mouse, or whole-genome replacement such as what is done with modern cloning methods, and is no more "spontaneous generation" than those are.

According to the Revised Interim Utility Examination Guidelines Training Materials (hereinafter "Utility Guidelines"), "When an applicant has specifically asserted that an invention has a particular utility, that assertion cannot simply be dismissed by the Office personnel as being 'wrong.'" Utility Guidelines, page 5. Likewise, it is not proper to simply conclude that a particular utility is not credible, particularly in the face of contrary evidence:

An assertion is credible <u>unless</u> (A) the logic underlying the assertion is seriously flawed, or (B) the facts upon which the assertion is based are inconsistent with the logic underlying the assertion. Credibility as used in this

context refers to the reliability of the statement <u>based on the logic and facts</u> that are offered by the applicant to support the assertion of utility. A *credible* utility is assessed from the standpoint of whether a person of ordinary skill in the art would accept that the recited or disclosed invention is currently available for use.

Utility Guidelines, page 5 (underlying added for emphasis). In the present case, the examiner's rationale for refusing to accept the factual evidence presented in support of the asserted utility is entirely premised on the characterization of the invention as being directed to "spontaneous generation," a term as loaded with meaning in the biological sciences as the term "perpetual motion" is in the physical sciences. The examiner never addresses the fact that evidence in the specification, and in the subsequently submitted Declarations in corroboration, indisputably shows the operability of the claimed invention. Instead, the examiner dismissed this evidence by saying that "said Declarations are not commensurate in scope with the instant claims." Paper 8, page 6. This is contrary to the examiner's own logic, however, as the basic premise underlying the rejection is that it simply is not possible to achieve the asserted result with the claimed method, while the examiner's dismissal of the evidence in support of utility acknowledges that the methods do function to obtain novel bacteria from cultured eukaryotic cells (i.e., it shows operability for some embodiments, but not for the "full scope" of the claims).1

¹The examiner does use the term "isolating" when describing what the evidence shows, and to the extent this is intended to imply that the method simply results in the isolation of contaminating bacteria, this is squarely contradicted by the evidence, which demonstrates within the limits of scientific proof that there were no contaminating bacteria in the starting cell cultures.

Reviewing the evidence in the record that supports utility, two Declarations under 37 C.F.R. § 1.132 were filed in the parent case, Serial No. 08/719,367, and re-submitted with the most recent Amendment in this case. One Declaration is by the inventor, Dr. Douglas Robinson, Ph.D., and one is by an independent scientist, Dr. Anton Steuer, Ph.D., who conducted a rigorous confirmation of the experiments reported in the present application. Both of these Declarations present independent corroboration of the utility of the claimed methods.

The Robinson Declaration presents a "Final Report" prepared by Microbiological Associates, Rockville, Maryland (hereinafter "MA") at the request of Dr. Robinson. The experiments requested by Dr. Robinson were for the purpose of reproducing the process described in the present application. Robinson Declaration, paragraphs 4-5; Steuer Declaration, paragraph 3. The Steuer Declaration presents additional detail regarding the work performed at MA. Dr. Steuer is the scientist who supervised the experiments by MA that corroborated the operability and utility of the claimed methods, and is an expert in the field of cell culturing techniques. Dr. Steuer also is one of the scientists employed by Microbiological Associates who signed the Final Report.

Robinson Declaration, Paragraph 5; Steuer Declaration, paragraph 2. The "Final Report" states in its Conclusion that

"Two runs involving the periodic reintroduction of an aerobic atmosphere during an anaerobic eukaryotic cell culture phase resulted in the isolation of bacteria, specifically *Bacillus licheniformis*. . . . The isolation of bacteria from eukaryotic cells subjected to alternating anaerobic/aerobic cell culture conditions provides supporting evidence for the hypothesis of *de novo* evolution of bacteria from eukaryotic cells. On the other hand, the possibility of environmental contamination as the source of the bacterial isolates cannot be absolutely eliminated. Environmental contamination is unlikely due to the cGMP compliance procedures and practices employed in the performance of

the sterility assays, which includes a stringent environmental and personnel monitoring program. Also, no tube, plate, or bottle inoculated with eukaryotic cell control samples or media control samples showed any microbial outgrowth. These negative results for all the numerous control samples tested minimized significantly the possibility of environmental contamination."

(emphasis added)

The work reported in the Final Report was carried out under tightly-controlled sterility conditions and GMP. The results showed that neither the eukaryotic cell cultures used, nor the media, nor the equipment, showed any detectable microbial contamination -- in other words, there were no bacteria in any of the starting materials used, and none were introduced during the experiments. The Final Report also shows conclusively that microorganisms having all of the morphological characteristics of bacteria were isolated from the culture at the end of each of <u>four</u> experimental runs.

Dr. Steuer's Declaration explains the rigorous standards employed during the testing procedure to ensure that the starting material was not contaminated and that contamination did not arise during the course of the cell culturing procedures. Steuer Declaration, paragraphs 3-4 & 6. The equipment and procedures used at MA for this work met or exceeded the most rigorous standards present in the industry (Steuer Declaration, paragraph 6), and complied with, among others, the U.S. FDA Good Laboratory Practice Regulations, the U.S. E.P.A. GLP's, the United Kingdom CLP Compliance Programme, and the Japanese GLP Standard. Steuer Declaration, paragraph 7.

Dr. Steuer explains why, in his professional opinion, the production of bacteria was not due to "contamination." Steuer Declaration, paragraphs 8-10. In Dr. Steuer's opinion, the Patent Office had "applied a requirement of 'proving' a lack of

contamination that is not applied by persons skilled in this field." Steuer Declaration, paragraph 8. It is Dr. Steuer's professional opinion that "any scientific inquiry wherein one must 'rule out' contamination, as set forth in the Office Action², is meaningless." Steuer Declaration, paragraph 8. As set forth in the Steuer Declaration, the claimed process was shown to produce bacteria upon anaerobic/aerobic culturing of virally-infected eukaryotic cells. Moreover, the report contains a Quality Assurance statement showing that FDA and EPA Good Laboratory Practices were followed. The report concludes that "[e]nvironmental contamination is unlikely," thus overcoming the Patent Office's position that the results were attributable to contamination.

Taken together, these Declarations establish the utility of the claimed methods, by demonstrating that they are, in fact, operative by any standard applied by persons of ordinary skill in the art. This evidence *cannot* be simply dismissed by the examiner, but must instead be rebutted by equally credible evidence or reasoned argument. This the examiner has not done, but has rather rested the entire rejection on the mischaracterization that the applicant is attempting to claim "spontaneous generation of life," followed by the assertion that since the claimed "spontaneous generation" simply is not possible, the bacteria produced <u>must</u> be the result of contamination. As the unrebutted evidence shows, this is an improper characterization of the invention and the assertion based thereon therefor is groundless. This rejection was therefore improper and should be reversed.

²Referring to the Office Action in the parent case, Serial No. 08/719,367.

C. Rejection und r 35 U.S.C. § 112, first paragraph (Deposit R quir m nt)

The examiner has maintained the requirement for a deposit in accordance with the Budapest Treaty. Paper 8, pages 6-7. This requirement, to the extent it is required at all, has already been met. Samples of the cells obtained in the work reported in the specification Examples have been deposited with the American Type Culture Collection in compliance with the Budapest Treaty, as stated expressly in the specification at page 8, lines 10-13. As none of the claims recite specific bacterial isolates, such deposit should not even be necessary for enablement. The specification further states at page 9, lines 26-28 that suitable starting materials are publicly available, and also provides at page 9, line 29 to page 10, line 2, reference to techniques which can be used to produce additional starting cell cultures. Thus, additional deposits of starting materials are not necessary. Finally, the specification specifically discloses the public availability of all of the eukaryotic cells lines used as starting materials in the Examples, as follows:

Cell line	<u>Availability</u>	Citation to Specification
RT-HCMV	ATCC CRL 11655	page 22, lines 20-22
procine cerebral microvascular endothelial	Robinson, et al.	page 27, lines17-19
L929	ATCC CCL 1	page 27, lines 19-20
murine lymphoma	ATCC TIB52	page 27, lines 20-21
SV-40 transformed human colon	ATCC CRL 1807	page 28, lines 5-6
human colon adenocarcinoma	ATCC HTB 38	page 28, lines 6-7

If the issue with regard to cell line deposits is that the applicant has somehow failed to make all the necessary statements on the record regarding compliance with the Budapest Treaty, something not entirely clear from the latest Office Action, the applicant is prepared to submit whatever formalities the Patent Office requires in this regard. The availability of these starting materials (which are in the ATCC catalogue and are not cells lines maintained by the applicant) is a matter of public record. However as stated, the applicant is prepared to submit whatever formalities are needed to satisfy the Patent Office in this regard. Therefore, this rejection as articulated in not appropriate and should be reversed.

D. Rejection under 35 U.S.C. § 112, first paragraph (Enablement)

The examiner has maintained the rejection of the claims as not being enabled under 35 U.S.C. § 112, first paragraph. The examiner asserts that the specification is enabling for methods of "isolating" a bacterium from aseptically cultured eukaryotic cells, but not for "producing" bacteria, or for "recovering any and all bacteria." Paper 8, pages 10-11. Again, the examiner improperly ignores the evidence of record that demonstrates that the claimed method functions as claimed to produce bacteria containing eukaryotic and/or viral genes from an aseptic culture of retrovirally-infected eukaryotic cells. The examiner insists, in the face of all the evidence to the contrary, that the bacteria produced are the result of contamination of the starting cultures.

Paper 8, page 11. The examiner requires that the applicant prove with 100% certainly that there was not a single contaminating bacteria anywhere in the process, a standard of proof that simply does not exist in science or reality. Rather than accepting the clear evidence that, within the limits of scientific detection (which are indeed very accurate),

there was no bacterial contamination at any point in the process, the examiner starts with the conclusion that what the applicant is claiming is impossible and therefor *must* be the result of contamination, and requires the applicant to demonstrate with absolute certainly that it is not.

This has never been the standard for enablement. By definition, this disclosure enables the claims because it teaches (indeed, demonstrates) how to employ the claimed methods to produce a bacterium. "The enablement requirement is met if the description enables any mode of making and using the claimed invention." Engel Industries, Inc. v. Lockformer Co., 20 U.S.P.Q.2d 1300, 1304 (Fed. Cir. 1991). The claims on their face recite methods for producing "a bacterium." Thus, in order to meet the enablement requirements of § 112, first paragraph, the specification need only teach a person of ordinary skill in the art how to produce "a bacterium" (Engel Industries, supra), which it clearly does. In fact, the Robinson and Steuer Declarations confirm and conclusively establish that the methods disclosed in the specification enable the production of a number of different kinds of bacteria. The claimed methods need not lend themselves to producing "any and all" bacteria (this is a limitation inserted by the examiner that does not appear in the claims); the claims do not recite methods for producing specific bacteria, or all bacteria, just a bacterium, any bacterium, generally. In re Angstadt & Griffin, 190 U.S.P.Q. 214, 218 (Applicants are not required to disclose every species of their invention, even in an unpredictable art.) The statement that "the claims lack specific method steps for the recovery of the bacteria" (Paper 8, page 11) is irrelevant -- the method does not necessarily require the isolation

of the bacteria, and the Patent Office has provided no reason why such a step is required for enablement.

Additionally, the Office Action makes clear that the examiner has fundamentally misconstrued the nature of the invention in making this rejection. At page 11, the examiner that "it is unclear that the claimed method would be suitable for the recovery of any and all bacteria, a few of which may be present, but not detectable by certain means." Similar statements throughout the Office Action make clear that the examiner refuses to accept, in the fact of contrary evidence, that the products of the claimed methods are not the result of bacterial contamination of the treated eukaryotic cultures. The specification clearly states that the methods result in the acquisition by eukaryotic cells of all of the morphological characteristics of prokaryotes, and that the production of bacteria is *not* due to the presence of bacteria in the eukaryotic cell cultures. See, e.g., Comparative Examples 1/A, 1/B, 1/C, D (specifically page 26, lines 13-18), and 2/A. The Examples all provide considerable detail regarding both precautions taken against incidental contamination, and controls to monitor whether contamination had in fact occurred -- the results all indicated that there was no contamination. The Declarations of record further confirm the accuracy of the specification on this point. Dr. Seuer in particular states that in his expert opinion, the position that the Patent Office took in the parent case, which is essentially the same as that taken in the present Office Action, "is not applied by persons skilled in the art," and such an inquiry is "meaningless" in the context of this invention. Seuer Declaration, paragraph 8. The assumption of the examiner underlying this rejection therefore is incorrect.

The examiner further states that the claimed method is unpredictable. Paper 8, page 11. However, the Declarations accompanying this response conclusively demonstrate that the claimed methods are indeed completely repeatable. The examiner asserts uncertainty about how the method works, stating that it is not clear whether eukaryotic cells are living or dead at some point in the process, and that bacteria are produced under "low oxygen conditions." Paper 8, page 11. However, in Newman v. Quigg, the Federal Circuit stated that:

"While it is not a requirement of patentability that an inventor correctly set forth, or even know, how or why the invention works . . . neither is the patent applicant relieved of the requirement of teaching how to achieve the claimed result, even if the theory of operation is not correctly explained, or even understood."

11 U.SP.Q. 1340, 1345 (Fed. Cir. 1989). See also Fromson v. Advance Offset Plate, Inc., 219 U.S.P.Q. 1137, 1149 (Fed. Cir. 1983) ("it is axiomatic that an inventor need not comprehend the scientific principles on which the practical effectiveness of his invention rests."). The disclosure of the specification, as confirmed by the experiments discussed in the Robinson and Seuer Declarations, leave no doubt that the methods do indeed work. This is all that is required under § 112.

The examiner asserts that it is unclear how one of skill in the art would determine and assure that the actual viral and/or eukaryotic genes are indeed intact genes picked up, rather than random fragments thereof, or how one would determine if the genes were integrated into the genome. Paper 8, page 12. These assertions again assume that the bacteria produced by the claimed methods are contaminants, which, as discussed above, they are not. The issues raised by the examiner with regard to the genes themselves are not material to the claims. Whether or not the genes (which

term by definition means an intact coding sequence,³ and is specifically defined as such at page 7, lines 8-12 of the specification), are intact is not pertinent given the accepted definition of a "gene," as is the issue of genomic integration, since the bacteria are formed from the eukaryotic cells. A person of ordinary skill in the art would recognize that any eukaryotic genes present in bacteria produced by the claimed methods would be intact, stable and integrated in the genome, because that would be their condition prior to performance of the claimed methods. In any event, methods for detecting, analyzing, evaluating and characterizing genes are routine procedures for the person of ordinary skill in the art.⁴

On the whole, the evidence of record clearly demonstrates that the claimed method work, and the examiner has presented no contradictory evidence or reasoned argument to rebut of this evidence. Rejection of the claims for lack of enablement therefor is inappropriate, and this rejection should be reversed.

E. Rejections under 35 U.S.C. § 112, second paragraph (Definiteness)

1. "Under low oxygen conditions" indefinite

The examiner maintained an earlier rejection of claims 1-29 as being indefinite in the use of the term "under low oxygen conditions." Paper 8, pages 12-13. The

³See, Lewin, B., Genes V, page 1242, Oxford University Press (1994), a copy of which is annexed for the Examiner's convenience.

⁴See, e.g., Sambrook, J., et al., Molecular Cloning, A Laboratory Manual, 2d ed., Chapter 9, Cold Spring Harbor Laboratory Press (1989). A copy of the table of contents for Chapter 9, which provides an outline of analytical techniques then available, was submitted with the previous Amendment filed June 24, 2002. The entire chapter is rather voluminous and not strictly necessary to support the applicant's arguments, but the applicant can provide the entire chapter if the Board so requires.

examiner asserts the term is not defined in the specification because the definition states that suitable anaerobic conditions include an atmosphere of 0-2 v/v% oxygen, merely identifying one of a multitude of possible concentrations, making it impossible to determine the metes and bounds of the claimed invention. Paper 8, page 13. The Federal Circuit has noted that "[m]athematical precision should not be imposed for its own sake; a patentee has the right to claim the invention in terms that would be understood by persons of skill in the field of the invention." Modine Mfg. Co. v. ITC, 75 F.3d 1545, ____, 37 U.S.P.Q.2d 1609, 1617 (Fed. Cir. 1996). Applicant submits that the term "low oxygen conditions" would be readily understood in the context of the invention by person of ordinary skill in the art, particularly in view of the definition of the term at page 9, lines 15-18 ("Preferably, the low oxygen conditions comprise alternating anaerobic culturing conditions with at least one brief period of exposure to an aerobic or microaerophilic condition."). The definition is clear, and uses terms having wellestablished meanings in the art - anaerobic (absence of oxygen), aerobic (presence of oxygen) and microaerophilic (very low levels of oxygen tolerated by microaerophilic organisms). The fact that the specification goes on to state that "aerobic conditions" "include" a particular range of oxygen concentrations does not render this definition vague - the definition comprises any aerobic conditions, with a preferred range of 0-2 v/v% oxygen. This is as precise as the subject matter permits. See Shatterproof Glass Corp. v. Libby-Owens Ford, Co., 758 F.2d 613, 624, 225 U.S.P.Q. 634, 641 (Fed. Cir. 1985) ("if the language is as precise as the subject matter permits, the courts can demand no more"). This rejection is improper and should be reversed.

2. Claims 2, 3 and 15 contradictory

The examiner has also maintained the rejection of claims 2, 3 and 15 as being vague and indefinite and confusing because the claims recite "subjecting the cells to an aerobic culturing step," yet depend from claims (in the case of claims 2 and 3) that recite culturing under "low oxygen conditions." Paper 8, page 13. The examiner asserts that since no "active steps" are defined to separate the two steps they remain contradictory and confusing. Id. The examiner's position is untenable in view of the express definition of "low oxygen conditions" in the specification at page 9, lines 15-18. The specification states that "[p]referably, the low oxygen conditions comprise alternating anaerobic culturing conditions with at least one brief period of exposure to an aerobic or microaerophilic condition." Thus, there is no contradiction between the claims because the embodiments recited in claims 2 and 3 are expressly contained within the definition of the conditions recited in the claim from which they depend. In the case of claim 15, this rejection makes even less sense, as the claim recites expressly a series of method steps:

'15. A method for producing a bacterium that contains a eukaryotic and/or viral gene, which comprises (a) culturing virally-infected eukaryotic cells under anaerobic conditions with at least one exposure to aerobic or microaerophilic conditions, (b) culturing cells from step (a) under aerobic conditions, and (c) isolating at least one bacterium that contains a eukaryotic or viral gene.

In the interest of expediting allowance of the claims, the applicant proposes amending claim 3 to recite "subjecting the cells to a <u>final</u> aerobic culturing step. This amendment is not believed necessary, but has been submitted concurrently herewith in the event

the Board considers it to be required to overcome this rejection. This rejection should be reversed.

3. Failure to set forth the invention

The examiner has issued a new rejection of claims 1-29 as failing to set forth the subject matter which the applicant regards as his invention. Paper 8, page 14. The examiner cites the applicant's submissions in Paper 7, filed June 24, 2000, wherein it is stated that the genome of the bacteria produced is eukaryotic in nature, in essence "deevolved" from the starting eukaryotic cell culture. The examiner concludes that the claims reciting "a single eukaryotic gene" thus do not describe this invention. Paper 8, page 15. The examiner again is resorting to semantics in order to support the rejection. The specification makes clear that the genome of the bacteria produced need not comprise the complete genome of the starting eukaryotic cells. Specification, page 7, lines 2-25. The genes might be altered, and the bacteria may also include viral genes, but the bacteria will contain at least one intact eukaryotic gene. Id. This is not at all inconsistent with the statements made by the applicant in Paper 7. First, this statement was made in response to the allegation that there was no evidence that the eukaryotic gene(s) present in the bacteria produced would be intact, stable and integrated into the genome (an issue irrelevant to patentability in any case, see section VIII.D, above), and was merely pointing out that since any eukaryotic gene present in the bacterium was derived from the starting eukaryotic cells, it would clearly be stable, intact and integrated into the genome. Second, the use of the phrase "at least one eukaryotic gene" does not exclude an entire intact genome. So, from either point of view, there is

no inconsistency between the applicant's statements in Paper 7 and the language of the claims. This rejection is improper and should be reversed.

4. "Derived," "evolved," "pleiomorphic" and "morphology" indefinite

The examiner has issued a new rejection of claims 24-29 as being indefinite. The examiner, however, has not provided any specifics for the inclusion of claims 26 and 28 in this rejection. Applicant assumes that the inclusion of claims 26 and 28 was an oversight.

The examiner has rejected claims 24 and 25 as being indefinite in the use of the term "derived," asserting that it is not clear what steps are required for "derivation." Paper 8, page 15. However, claims 24 and 25 specifically reference the methods of claims 1 and 15, respectively. Thus, the way in which the claimed cells are "derived" is expressly included in the claim. The examiner has also rejected claims 24 and 25 as being indefinite in the use of the term "evolved." Id. The term is well-understood in the art to mean "changed over time," or a similar meaning; claims 24 and 25 specifically recite that the gene in the claimed cell evolved from a eukaryotic cell treated in accordance with the methods of claims 1 and 15, respectively. The clear meaning is thus that the gene in the claimed cell has been changed from the gene of the starting eukaryotic cell by application of the process of either claim 1 or claim 5. This is as clear a recitation of the invention as the subject matter, and the English language, permits. The examiner also has rejected claims 24 and 25 as indefinite in the use of the term "pleiomorphic cell." Id. This term, synonymous with "pleomorphic," and "polymorphic" in this context, has a well-established meaning. See Webster's Third New International Dictionary definitions of "pleiomorphic," "pleomorphic" and "polymorphic" at pages 1739, 1740 and 1759 (copies attached for the Board's convenience). Contrary to the examiner's assertion, all cells are <u>not</u> pleiomorphic by nature – not all cells exist in several distinct forms or are capable of assuming varying forms. The use of the term in the specification is in complete accordance with the accepted meaning. <u>See, e.g.,</u> specification, page 29, lines 10-20 ("morphologies that appear to be of neither a prokaryotic nor a eukaryotic nature were often observed ..."; "... various bizarre morphologies were often observed."). Furthermore, the examiner's statement that "it is unclear how the cell of the instant claim differs from any other cell since all cells are pleiomorphic in nature" (Paper 8, page 15) is not only factually baseless (see above), but also misleading, because the claims contain numerous additional elements that clearly distinguish the claimed cells from other cells such that the distinction does not depend only on the term "pleiomorphic." These rejections are improper and should be reversed.

The examiner has rejected claims 27 and 29 as being indefinite in the use of the term "morphology that is neither prokaryotic nor eukaryotic." Paper 8, page 15. The examiner asserts that it is unclear what is meant by the phrase since "prokaryotic" and "eukaryotic" are taxonomic terms and not morphology types. This assertion is simply incorrect. There are certain morphologies that are well-established as being characteristic of prokaryotic or eukaryotic cells. For example, the presence of a nucleus and other sub-cellular organelles such as mitochondria and endoplasmic reticulum is accepted as a characteristic "eukaryotic" morphology, and the absence of the same as a "prokaryotic" morphology. Also, certain cell shapes are accepted as characteristic "morphologies" of prokaryotic cells, for example the "coccoid" (spherical) form and the

"baccillus" (rod-like) form. Furthermore, when referring to the "morphology" of a cell, it is generally understood in the art that one is referring to the over-all morphology unless specified otherwise (for example, by discussing "morphological features"). Thus, the statement that the "morphology" of the cells is neither prokaryotic nor eukaryotic would be understood to mean that the overall morphology of the cell is not consistent with either, because certain key features are missing, or there is an unusual combination of features not found in either prokaryotes or eukaryotes. Discussion of cell morphology, consistent with this accepted meaning, appears at pages 2-5 and 28-29 of the specification. Any doubt as to the meaning of this phrase as used in the claims is removed by the disclosure, which states that the ultrastructure of isolated cells was extremely variable (page 29, lines 10-12), that the morphology was "of neither a prokaryotic nor a eukaryotic nature" (page 29, lines 16-17), and often "bizarre" (page 29, lines 21-22). Again, the language used in the claims is as definite as the subject matter permits and would be readily understood by a person having ordinary skill in the art. Therefor this rejection is improper and should be reversed.

F. Rejections under 35 U.S.C. § 112, second paragraph (Written Description)

The examiner has rejected claims 24-29 as containing subject matter that is not described in the specification. The examiner asserts that the claim limitation that the cell is not a transgenic cell is not supported by the specification. Paper 8, page 14. Examiner is applying an inappropriate *in haec verba* test for written description.

Although the specific words "not a transgenic cell" do not appear in the specification, the specification as a whole reasonably conveys to a person having ordinary skill in the

art that the method indeed employs cells that are not transgenic, and that this method was in the possession of the inventor at the time the application was filed. This is sufficient under the second paragraph of § 112:

"The test for determining compliance with the written description requirement is whether the disclosure oif the application as originally filed reasonably conveys to the artisan that the inventor had possession at the time of the later claimed subject matter, rather than the presence or absence or absence of literal support in the specification for the claim language."

In re Kaslow 217 U.S.P.Q. 1089, 1096 (Fed. Cir. 1983) . Put another way, if a person having ordinary skill in the art would immediately discern the limitation from the original disclosure, the written description requirement is satisfied. Purdue Pharma L.P. v. Faulding Inc., 56 U.S.P.Q.2d 1481, 1483 (Fed. Cir. 2000) (no in haec verba test for written description - limitation need only be conveyed with reasonable clarity). The present specification clearly states that an aspect of the invention is a method for producing bacterial cells expressing animal and/or viral genes that does not require any step to introduce these genes into bacteria to create transgenic bacterial cells. See specification page 6, lines 24-30; page 9, lines 5-14; page, line 27 - page 11, line 27. The present specification also describes in detail the claimed methods, with specific examples wherein the cells produced clearly are not transgenic cells because nowhere in the methods used in these examples is there a step where a transgene is introduced into bacterial cells. See, e.g., Examples 1-5. A person having ordinary skill in the art would understand that this disclosure described cells that are not transgenic cells because they are not the product of traditional molecular biological transformation techniques. This rejection therefore is inappropriate and should be reversed.

CONCLUSION

For all of the foregoing reasons, the final rejections applied to the claims are without merit. Applicant respectfully requests that these rejects be reverse, and that the Board direct the examiner to issue a favorable action on the claims.

RESPECTFULLY SUBMITTED,							
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Attachments: Appendix A, copy of claims on appeal.

2149-107 appeal brief.wpd

Appendix A

Copy of the Appealed claims

- 1. A method for producing a bacterium that contains a eukaryotic and/or viral gene, which comprises culturing virally-infected eukaryotic cells under low oxygen conditions to produce a bacterium containing a eukaryotic and/or viral gene.
- The method according to claim 1, wherein said low oxygen conditions comprise anaerobic culture conditions with at least one exposure of the cells to aerobic or microaerophillic culture conditions.
- 3. The method according to claim 2 which further comprises subjecting the cells to an aerobic culturing step.
- 4. The method according to claim 2, wherein said anaerobic culture conditions comprise an atmosphere containing less than or equal to 1 v/v% oxygen, based on the total volume of atmosphere.
- 5. The method according to claim 4, wherein said atmosphere contains less than 0.1 v/v % oxygen, based on the total volume of atmosphere.
- 6. The method according to claim 1 wherein said virally-infected eukaryotic cells are retrovirally-infected mammalian cells.
- 7. The method according to claim 6, wherein said mammalian cells are human cells.
- 8. The method according to claim 1, wherein said eukaryotic cell is a mammalian, avian or fish cell.
- 9. The method according to claim 8, wherein said eukaryotic cell is an endothelial cell.

- 10. The method according to claim 1, wherein said eukaryotic cell is a mammalian brain capillary endothelial cell.
- 11. The method according to claim 1, wherein said virally-infected cell is infected with a virus selected from the group consisting of the murine L-cell virus, simian immunodeficiency virus (SIV), human immunodeficiency virus (HIV), Ableson murine leukemia virus and Moloney murine leukemia virus.
 - 12. The method according to claim 11, wherein said virus is the murine L-cell virus.
- 13. The method according to claim 1, wherein said culturing step is carried out at a temperature between about 20 and about 50°C.
- 14. The method according to claim 1, wherein said culturing step is carried out at a temperature of about 37°C.
- 15. A method for producing a bacterium that contains a eukaryotic and/or viral gene, which comprises (a) culturing virally-infected eukaryotic cells under anaerobic conditions with at least one exposure to aerobic or microaerophilic conditions, (b) culturing cells from step (a) under aerobic conditions, and (c) isolating at least one bacterium that contains a eukaryotic or viral gene.
- 16. The method according to claim 15, wherein aerobic culturing step (b) is carried out in an atmosphere containing at least 0.1 v/v% oxygen, based on the total volume of atmosphere.
- 17. The method according to claim 16, wherein said atmosphere contains more than 1 v/v% oxygen, based on the total volume of atmosphere.
- 18. The method according to claim 15, wherein said virally-infected eukaryotic cell is a retrovirally-infected mammallian endothelial cell.

- 19. The method according to claim 15, wherein said virally-infected eukaryotic cell is a human brain capillary endothelial cell infected with the murine L-cell virus.
- 20. The method according to claim 1, further comprising filtering the cells cultured in step (a) prior to said aerobic culturing step (b).
- 21. The method according to claim 20, comprising filtering the cells through a 0.1 to 0.8 μ m filter.
 - 22. The method according to claim 21, wherein said filter is 0.1 to 0.45 μ m.
 - 23. The method according to claim 22, wherein said filter is 0.22 μ m.
- 24. A pleiomorphic cell that is not a transgenic cell, and is derived from a eukaryotic cell, containing at least one gene evolved from the genome of said eukaryotic cell, prepared by a process according to claim 1.
- 25. A pleiomorphic cell that is not a transgenic cell, and is derived from a eukaryotic cell, containing at least one gene evolved from the genome of said eukaryotic cell, prepared by a process according to claim 15.
 - 26. A cell according to claim 24 that is a bacteria.
- 27. A cell according to claim 24 that has morphology that is neither prokaryotic nor eukaryotic.
 - 28. A cell according to claim 25 that is a bacteria.
- 29. A cell according to claim 25 that has morphology that is neither prokaryotic nor eukaryotic.

Webster's Third New International Dictionary

OF THE ENGLISH L'ANGUAGE UNABRIDGED

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An excuse for pleasure-seekers to see the sun rise —Linton. Wells)

| pleasuring n -s [fr. gerund of *pleasure] 1: an act or instance of taking or giving pleasure (changed from earning their living from farming ... to the business of ~ —Mary H. Vorse) 2: a pleasure trip: VACATION
| pleasuring ad [fr. pres. part. of *pleasure]: designed or used for pleasure (taking their ease in great ~ grounds where the wilderness is preserved —R.M.Yoder)
| pleas.ur.ist \('\pie.t.m.'\sigma' \sigma' \) pleas ("\pie.t.m.'\sigma' \sigma' \) pleats ("\pie.t.m.'\sigma' \sigma' \) pleats ("\pie.t.m.'\sigma' \sigma' \) a preserved —R.M.Yoder)
| pleas \('\pi' \) pleats ("\pie.t.m.'\sigma' \sigma' \sigma' \) pleats ("\pie.t.m.'\sigma' \sigma' \sigma' \sigma' \sigma' \) pleats ("\pie.t.m.'\sigma' \sigma' \s (an excluse for pleasure-seekers to see the sun rise — Linton Wells)

(an excluse for pleasure-seekers to see the sun rise — Linton Wells)

(a) excluse for pleasure seekers to see the sun rise — Linton Wells)

(b) pleasuring n-s [fr. gerund of *pleasure] 1: an act or instance of taking or giving pleasure (changed from earning their living from farming... to the business of ~ — Mary H. Vorse — Ma

character, manners, or style: CRUDENESS, VULOARITY (a Greek philosopher in the midst of foreign ——Irich Statesman) (scorns no business for its ——Thomas Carlyle) ple-be-lan-lize \(^12-n\), \(^12\) \(

are scattered throughout the tissue of perithecia or similar structures pleo-ten-chy-ma \plek'tenkomo\ n -s [NL, fr. plect + -enchyma]; a parenchymatous tissue formed by massed and twisted filaments or tubular cells esp, in fungi and lichens — compare PROSENCHYMA, PSEUDOPARENCHYMA — pleo-ten-chyma-tous \plek'tenk, implea-as\ adi [NL 'Plectognathi or relating to the Plectognath.] : of or relating to the Plectognath | nplectognath \ n -s : a fish of the order Plectognathi | plectognath \ n - n -s : a fish of the order Plectognathi | plectognathi | nplectognathi | nplec

with the cross recovery as a said plec-top-tera | an insect of the order Plectoptera | an insect of the order Plectoptera | plec-top-tera | pl

united and use. being more or less coextensive with Ostariophysis – plec-to-stelle \piekta,stel alor or stelle \piekta, and plect-to-stelle \piekta,stell alor or stelle \piekta, and the hexage arranged in use. parallel plates

TRUM 1; PLECTRUM — NI — 3 EF, fr. 1. plectrum — more at PLECTRUM plect-tride and continuous plect-tride and the plect-tride in the form of a drumstick plect-tride. The plectrum — NI — delta in a delta plectride in the plectride in the plectride of the plectride in the plectride in the plectride of the pl

guaranty of the good intentions of the person or agency performing the yielding (giving over their children as hostages to the invaders) ** **P-ING/-S [ME pleggen to become surety for, fr. MF plegier, fr. OF, fr. plege, n.] **v 1 1: to give as a pledge control of the pleggen to become surety for, fr. MF plegier, fr. OF, fr. plege, n.] **v 1 1: to give as a pledge of eposit (as a chattel) in pledge or pawn: make a pledge of eposit (as a chattel) in pledge or pawn: make a pledge of the pawn, specif: to assign as security for the repayment of a loan — composed to goodwill or favor by or in drinking to: aobst: to control of the pledge of the position of the pledge of th

(Ir. the stem of plessein to strike) + NL -ia]: paralysis of specified nature (paraplegia)
-ple-sp 'pleje, -ji, in comb form -es [NL -plegia]: paralysis of a specified nature
ple-iad 'pled also 'plid \ n-s [F Plélade, a group of 7 16
cent. Fr. poets, fr. MF, fr. Plélade, a group of 7 tragic por
of a specified nature
ple-iad 'pled also 'plid \ n-s [F Plélade, a group of 7 tragic por
of ancient Alexandria, fr. GK Pleiades, Pletlades, pl.,
Pleiades, Pletlades, 7 stars in the constellation Taurus];
group or cluster of illustrious or brilliant persons or thin
usu. seven in number (educated a brilliant \sim of great maste
of painting \(-Encyc. Americana \)
plei-idae 'pledde', n pl. cap [NL, fr. Plea, type genus ()
GK plein to sail, float, swim \(+ \data \)
de more at FLOW];
widely distributed family of small aquatic bugs
'plein air 'plan \(- \) I. F. lit., full air]; outdoor daylight (
paint in plein air) (to render the high tonal values of the loc
plein air \(- \) adj \(1 \): relating to the method, action, or prouct of painting in outdoor daylight \(2 \): of, relating to,
constituting a French art movement starting about 1863 white
attempted to represent effects of outdoor light and air no
beervable in the studio
plein-air-isim \plain(a): risma \quad or plein-air-isme \plein
eres(m²), \(\frac{\varphice}{\varphice} (m²), \(\frac{\varphice}{\varphice} (m

nethod, or practice of plein air painting plein leu \plai^\ n, often cap P& [F, lit, full play]: in pie organ including the unison, octave, an fifth pleio- or pleo- or plio- comb form [Gk pleiön, pleön — more in the pleio- or pleo- or plio- comb form [Gk pleiön, pleön — more in the pleio- or pleo- or plio- comb form [Gk pleiön, pleön — more in the pleio- or pleo- or plio- comb form [Gk pleiön, pleön — more in the pleio- or pleo- or plio- comb form [Gk pleiön, pleön — more in the pleio- or pleo- or plio- comb form [Gk pleiön, pleio- har high pressure pleio- or in the pleio- or pleio- plei

Roman Catholicism: a remission of the entire temporal punishment due to sin.

plenary inspiration n: divine inspiration covering all subjects dealt with — compare VERBAL INSPIRATION

plene \[
\text{plene} \] viplene \[
\text{dealt} \] with — compare VERBAL INSPIRATION

plene \[
\text{plene} \] viplene \[
\text{dealt} \] with — compare VERBAL INSPIRATION

plene \[
\text{plene} \] viplene \[
\text{dealt} \] with — compare verbal in the plene in version in the subjects dealt in the plene in the pl



(00

by the lake the daffodils were now in their — Victoria Sackville-West) (will ... gain pleasure and profit in ~—H.M. Parshley)

plenty () dol [ME plente, ft. plente, n.] 1: ample in amount or supply: plenty (the plente) ft. plente, n.] 1: ample in amount or supply: plenty (the plente) ft. plente, n.] 1: ample in amount or supply: plenty (the plente) ft. plente, n.] 1: ample in amount or supply: plenty (the plente) ft. plente, n.] 1: ample in amount or supply: plenty (the plente) ft. plenty or number (who has coiles ~ to dispose of cheap—Jeremy Bentham) br. AMPLE, MANY: more than enough (the could get ~ men ... to the plenty (the plenty) ft. plenty (the plenty) ft. plenty (there is ~ work to be completely (the plenty) ft. plenty (the style is ~ but not about themselves JL.Phelan) (her style is ~ but not about themselves Jlenty) ft. plenty (the plenty) ft. plenty (the plenty) ft. plenty (the plenty) plenty (the

Denum ventilation n: a system of ventilation that applies the motive force at the inlets, drives the air through the rooms which become plenums, and avoids the incoming of cold drafts

plenum ventilation n: a system of ventilation the motive force at the inlets, drives the air through the rooms which become plenums, and avoids the incoming of cold drafts pleo—see PLEIO—ple-o-chro-ic \pleo-ichro-ic \pleo-ichro-ich

ple-o-mor-phous \;==!morfes\ adj [ISV pleomorphism -ous] : PLEOMORPHIC
ple-o-mor-phy \'-s,morfe\ n -ES [pleomorphous + -y] : PLEO-

iteration 2: SUPERFLUTTY (a ~ or overflow of that great kindness — Samuel Purchos)
ple-0-naste \ple_nast\ n = S[F, fr. Gk pleonastos abundant, fr. pleonaste \ple_nost\ n = S[F, fr. Gk pleonastos abundant, fr. pleonaste \pleonast\ n = S[F, fr. Gk pleonastos abundant, fr. pleonaste \pleonast\ n = S[F, fr. Gk pleonastos abundant, fr. pleonaste \pleonaste \pleonast

brown muriform ascospores in scattered or gregarious perithecia ple-0-spo-ra-ce-ae \niesaspa'rāsē,ē\ n pl, cap [NL, fr. Pleospora + aceae]: a family of ascomycetous fungi (order Sphaeriales) that is sometimes combined with Mycosphaerel-laceae and that includes parasitic fungi which cause stem or leaf spot diseases or rots of economic plants pler-er-gate \pilitar,gāt\ n [Gk plērēs full + E ergate — more at FULL]: REPLETE ple-ro-cer-coid \niesaspa pler-saspa \niesaspa \niesaspa pler-saspa \niesaspa pler-saspa \niesaspa \niesaspa

the uncreated monad or dyad from which they nave proceeded 2 [NL, fr. LL, fullness]: PLEROME — pile-ro-matic \pipiro-imad-ik\ adj pleroma violet n: a moderate purple that is bluer and duller than manganese violet or heliotrope (sense 4a) and bluer than average amethyst ple-rome \pipirōm\ also ple-rom \pipiroma \pipirom\ also ple-rom \pipiroma \pipiroma \pipiroma \pipiroma \pipirom\ also ple-rom \pipiroma \pipirom

tissues wood restanting from excessive and uneven grown of the pletho-rite \ 'plethorik, ple'thor, 'thär-, -rēk\ adj [LL pletho-ricus, fr. Gk plēthōrikos, fr. plēthōra plethora + -ikos -ic] 1: marked by plethora (a ~ condition) 2: marked by excess or profusion (that ~ opulence -Astalic Annual Register) (~ volumes which slumber in decorous old libraries -J.H. Burton)

volumes which slumber in decorous old libraries —J.H.
Burton)
pleth-0-Ty \plethorE\ n-es [fr. plethoric, after such pairs as E
allegoric: allegory] archaic: \text{PLETHORA} (the state of the nation
is full even to \times —Edmund Burke)
pleth-ron \plethorn\ n, pl pleth-ra\ -ra\ [Gk] 1: an ancient
Greek unit of length equal to 100 Greek feet or 101.2 modern
feet 2: a unit of area equal to one square plethron
plethys-mo-gram \plothizm_gram, \sim-\ n [ISV plethysmo-fitymo-(fr. plethysmograph) + -gram]: a tracing made by a
plethys-mo-graph \raf, -raf\ n [ISV plethysmo- (fr. Gk
plethysmos multiplication, increase, fr. plethynein to increase,
fr. plethys, plethos mass, magnitude) + -graph; orig, formed as
fr. plethys, plethos mass, magnitude) + -graph; orig, formed as
fr. plethys, plethos mass, magnitude) + -graph; orig, formed as
fr. plethys. plethos mass, magnitude)
for original plates of an organ or limb and in the amount
of blood present or passing through it

plēthysmos multiplication + NL thallus]; a dwarf filament thallus occurring in the life cycle of various brown algae: bearing at what appears to be a juvenile stage either uniloct or plurilocular sporangia
pleur- or pleuri- or pleuri- comb form [NL, fr. L, fr. Gk, s. rib, fr. pleura] 1 a: pleura (pleurotomy) (pleurisepti (pleurogenic) b: pleura and (pleuropericarditis) (pleurod) 2: side: lateral (pleurite) (pleurocentrum) 3:

the pleura of the pleura (pleurectomy) (pleuriseptic (pleuroenic) b. pleura and (pleuropericarditis) (pleupedal) 2: side: lateral (pleurite) (pleuroeentrum) 3: (pleural) 1 pleural (pleuroeentrum) 3: of two-walled sacs of serous membrane each lining one late half of the thorax, having an inner layer closely adherent to corresponding lung, reflected at the root of the lung to forn parietal layer that adheres to the walls of the thorax, the pecardium, upper surface of the diaphragm, and adjacent parand containing a small amount of serous fluid that minimit the friction of respiratory movements b: the membrant issue making up the pleurae 2 [NL, fr. Gk]: a laters located body part; specif; PLEURON 7 pleural of PLEURON or of PLEURUM 1 pleura (pleura (pleura) pleura-can-thea (plura'kan(i)thēs) or pleu-ra-can-thea (plura'kan(i)thēs) or pleu-ra-can-thu-(pleura-can-thu-qleura-qleura-

sect wing pleural sclerite n: any of several plates of the pleural area.

the insect integument
pleur-ap-o-phys-i-al \pluirapo; fizēs \ adj [pleurapophysis
-al]: of, relating to, or having the characteristics of a pleuri

pleur-ap-o-phys-i-al \plujtapo-fizēol \adj [pleurapophysts \-al]: of, relating to, or having the characteristics of a pleur pophysis
pleur-apophy-y-sis \,pluro-pliss\s\ n \ [NL, fr. pleur-apophysis]: a laterally or more or less ventrally directed process or appendage of a vertebra forming a rib or part corn sponding to a rib: a rib that is a part of a vertebra pleur-ric \pleuriss and if \ n = pleura side, rib + ikos-ic! \ pleura side, ric | pleura side, rid | pleuriss \ pleuriss \, pleura side, rib + ikos-ic! \ pleurall | pleurall | pleuriss \, pleura side, rib + ikos-ic! \ pleurall | pleurall | pleuriss \, pleura side, rib + ikos-ic! \ pleurall | pleu

LL pleuriticus, fr. Gk pleuritikos, fr. pleuritis + -ikos-ic]: of relating to, or suffering from pleurisy pleurit-its \plilitrīd-s\ n, pl pleurit-it-des \-irid-3,dēz\ [L. ; PLEURSY pleuro-— see pleura-pleuro-— see pleura-pleuro-— see pleura-pleuro-— see pleura-pleuro-prachid \-plura-brākēa\ n, cap [NL, fr. pleur-+brachid]: a genus (the type of the family Pleurobrachidae) of globose or ovoid relatively firm-bodied ctenophores pleu-ro-branch \-plura-brank\ also pleu-ro-branchia \-**ea-brachid]: a genus (the type of the family Pleurobrachidae) of globose or ovoid relatively firm-bodied ctenophores pleu-ro-branchia \-**ea-brachid]: a gill of a crustacean arising from the side of the thorax — compare Poddbranchi-ate \-**eā\ [NL, fr. pleur-+ branchid]: a gill of a crustacean arising from the side of the thorax — compare Poddbranchi-ate \-**eā\ adj pleu-ro-branchida \-**e-"prankēa\ or pleu-ro-branchi-ate \-**eā\ adj pleu-ro-branchida \-**e-"prankēa\ or pleu-ro-branchi-ate \-**eā\ adj pleu-ro-branchida \-**e-"prankēa\ or pleu-ro-branchi-ate \-**eā\ adj pleu-ro-branchida \-**e-"prankēa\ or pleu-ro-branchidae \-**eā\ adj pleu-ro-branchidae \-**ea-branchidae \-**ea-bran

not developed—compare THIARA—pleu-foc-er-old\-sa,roid\
addient-o-cerebral \;plurō+\ adj [pleur-+ cerebral]: connecting the pleural and cerebral ganglia of a mollusk
pleu-foco-cus \;\plurō-k'aks\. [NL, fr. pleur-+ -coccus]
syn of protococus
pleu-fo-di-ral \;\pluro'dira\ n pl, cap [NL, fr. pleur-+ -dira (fr.
Gk derê, delrê neck)—more at DER-]: an extensive group of
freshwater turtles in which the neck cannot be retracted, but is
bent laterally beneath the front of the carapace—compare
MATAMATA—pleu-fo-di-ran \;\r'-sidiran\ adj or n — pleufo-dire \(\frac{1}{2} \cdot \c

adj poly-karyon also poly-caryon \"+\ n [NL, fr. poly-+ karyon]: a multinuclear cell or individual poly-kary-01-10 \+!kare\"id-ik\ adj [poly-+ kary-+-otte]: having many nuclei or cells with many nuclei poly-lem-ma (pale]-lem-, 12\"\ n = [poly-+ -lemma (as in dilemma)]: an argument analogous to a dilemma in which many (as more than three) alternatives are presented in the major premise

major premise
poly-inignal \palic -la+\ adj [poly- + lingual] : MULTILINGUAL (~ area) (a ~ journal)
poly-literal \ "+\ adj [poly- + literal] 1 : POLYGRAPHIC
(~ transposition) 2 : representing each letter by a polygraph (~ transposition) 2: representing each letter by a polygraph (~ substitution) poly.literally ("+\ adv: in a polyliteral manner: so as to be

poly-lith \'== lith\ n = [poly-+-lith]: a megalithic structure (as a dolmen or stone circle) made of several or many stones

poly-lith *_s,lith \n -5 lpoly- + -lith! : a megalithic structure (as a dolmen or stone circle) made of several or many stones — compare MONOLITH
poly-lith-to \!.*_ilithik\ adj [poly- + -lithic] : composed of several or many stones or kinds of stone (a ~ deposit)
poly-mas-tia *_*_* massiz>\ also poly-mas-ty *_**_**_*iz\ n, pl
polymastias also polymasties [NL, fr. poly- + -mastia]
: the condition of having more than the normal number of breasts — poly-mas-tic *_**_*ix\ adj
poly-mas-ti-da *_**_mastia'\ or poly-mas-ti-ga\ or poly-mas-ti-go-ta *_*Od-*\[n\]\. [NL, irreg. fr. Polymastig-, Polymastil_\; zw of Poly-mas-ti-go-ta *_*Od-*\[n\]\. [NL, irreg. fr. Polymastig-, Polymastil_\; zw of Poly-mastig-\; na*_*, masti-y\[n\]\. [n]\. ap [n]\. cap [NL, fr. Poly-mastig-, Polymastix, genus of liagellates (fr. poly- + Gk mastig-, mastix whip) + -lna — more at MASTIG-]: an order of small plastic usu parasitic flagellates (sub-class Zoomas-tigina) having several flagella and including various medically or economically important forms (as members of the genera Costia, Chilomastix, Giardia, Hexamita, and Trichomonas)
- poly-mas-ti-gio *_**_*mastig-jin\ adj [alter. of earlier poly-mastigiae [tr. poly-mastigiae]: of or relating to the Polymastigiae
2 [NL Polymastigota]: of or relating to the Polymastigina
1 poly-math *_**_math\ n - s [Gk polymaths knowing much, in the content of the polymaths of the poly-math *_**_math\ n - s [Gk polymaths knowing much, in the poly-math *_**_math\ n - s [Gk polymaths knowing much, in the poly-math *_**_math\ n - s [Gk polymaths knowing much, in the poly-math *_**_math\ n - s [Gk polymaths knowing much, in the poly-math *_**_math\ n - s [Gk polymaths knowing much, in the poly-math *_**_math\ n - s [Gk polymaths knowing much, in the poly-math *_**_math\ n - s [Gk polymaths knowing much, in the polymaths knowing much, in the poly-math *_**_math\ n - s [Gk polymaths knowing much, in the polymaths knowing much, in the polymaths knowing much, in the polymath knowing much, in the pol

polysimals the court of the masting state of the Polymastignia 2 [NL Polymastignia]: of or relating to the Polymastignia 2 [NL Polymastignia]: of or relating to the Polymastignia 3 polymastignia (** n. s.; a flagellate of the order Polymastignia polymastignia) (** n. s.; a flagellate of the order Polymastignia polymath (** n. s.; a flagellate of the order Polymastignia polymath (** n. s.; a flagellate of the order Polymastignia polymath (** n. s.; a flagellate of the order Polymastignia polymath (** n. s.; a flagellate of the order polymastignia polymath (** n. s.; a flagellate of the sub-critics are ~* s. R. G. Davis) — called also polyhistor (** latended in many fleds — compare ERUDITE (masters of the sub-flagellate of the sub-flagellat

[ISV, prob. back-formation fr. polymerization]: a product of polymerization 'NOLYMER po-lym-er-i-za-tion' \pa_a,limora'zāshan, pālām-, pālēm-, rī-z-\pa_n - s - [ISV polymer + -ization] 1 a : a chemical reaction in which two or more small molecules combine to form larger molecules that contain repeating structural units of the original molecules and that have the same percentage composition as the small molecules if the small ones were all of the same kind: the union of monomers to form polymers — see Addition POLYMERIZATION, CONDENSATION POLYMERIZATION, CONDENSATION POLYMERIZATION, CONDENSATION POLYMERIZATION, CONDENSATION 7 3: reduplication of parts in the animal body po-lym-er-ize \(\frac{1}{2} \) pa'lima-riz- [pālām-, 'pālēm-\vb -ED/-INO/-s see -ize in Explan Notes [polymer + -ize] vr: to combine (small molecules) chemically into larger or esp. very large molecules from small molecules: undergo polymerization po-lym-er-iz-er \(\frac{1}{2} \) va-5: an operator of polymerization coulpment

po-lym-er-ous \po-limpros\ ad/[poly- + -merous] 1: having many parts or members in a whorl 2 [polymer + -ous]

many parts or members in a whorl 2 [polymer + -ous] : POLYMERIC | polymer tempera n : an aqueous plastic-based paint used

: POLYMERC!

polymer tempera n: an aqueous plastic-based paint used esp. in fine art polymerty \pa^2\text{limor}\text{Z}, \text{pal}\text{Pal}\text{Limor}\text{Pal}\text{Pa

isoprene occurring naturally in a cis form as the rubber hydrocarbon and in the corresponding trans form as gutta and also produced synthetically in several forms poly-isotopic *+\ adj [poly-+ metric]: relating to, exhibiting, involving, or employing a variety of meters poly-isotopic *+\ adj [poly-+ lisotopic]: of, relating to, or consisting of more than one isotope poly-kar-yo-cyte _nightharpoonup \; \text{aryo-cyte}_nightharpoonup \; \text{aryo-cyte}_

polymeaby polimeates needs and sariety of meters polymeaby polimeaby needs as spolymeric + yl; the combination of different prosodic meters; esp: the use of different meters in different lines of the same poem or the same stanza poly-microbic or microbial): of, relating to, or caused by several types of microorganisms
poly-migrapte or poly-mign.itte \phile poly- + microbic or microbial): of, relating to, or caused by several types of microorganisms
poly-mig-nyte or poly-mig-nite \phile poly- + microbic or microbial): of, relating to, or caused by several types of microorganisms
poly-mig-nyte or poly-mig-nite \phile poly- + mis-nyte or poly-mig-nite. \phile poly- + mis-nyte of the metals of the cerium group with iron and calcium poly-mix-la \phi-mix-sax \n, cap (NL, fr. Gk, mixture of many components, fr. poly- + mixis act of mixing (fr. mignynal to mix) + i-vy |: a genus of small deep-sea berycoid fishes co-extensive with the family Polymixidae and resembling the squirreflishes but having smooth scales and a pair of barbels on the chin — poly-mix-1-id \phi-si-sed(n or ad) polyminal \poly-minal \poly-minal

polymorphonuclear \\ n = s: a polymorphonuclear leukocyte
polymorphonuclear \\ n = s: a polymorphonuclear leukocyte
polymorphonuclear + ate]: polymorphonuclear | add ['polymorphonuclear + ate]: polymorphonuclear | add ['polymorphonuclear + ate]: polymorphonuclear | add ['Gk polymorphon multiform fr. poly- + -morphos-morphonus]: having or assuming various forms, characters, styles, or functions (a ~ god): as a: polymorphonus-perverse \\ ': e': e': e': e': a' a v - polymorphonus-perverse \\ ': e': e': e': a': a' a v - polymorphonus-perverse \\ ': e': e': a': a' a v - polymorphonus-perverse \\ ': e': e': a': a': a' a d \\ : retaing to or exhibiting infantile sexual tendencies in which the genitals are not yet identified as the sole or principal sexual organs nor coitus as the goal of erotic activity and which are a basis for pregenital libidinal fixation
poly-mor-phy \\ 'palie,morfe, -la,m-\ n -es [ISV polymorph + -y]: polymorph \\ -y': polymor-pha \\ '-e': mgl'a' = n or -ali: having many cells in each quadrant of a cross-section — used of the arrangement of muscle cells in a nematode worm
poly-my-ar-i-aly \\ '*-,mnlard-d\ n - es [polymy-arian + -ity]: the condition of being polymyarian
poly-my-odi \\ 'palie,mlads mightan \\ 'n m, n, n, ap [NL, fir. poly-+my-odi \\ 'palie,mlads manny armouse, muscle) — more at Mouse] in former classifications: a group of birds nearly equivalent to Passeres — poly-my-odi \\ '*-,e'', in old \\ 'adi ['poly-+ my + -old] 1: having manny syringeal muscles 2 [NL Polymyodi + E old]: Poly-MyODIMS
poly-my-ositis \\ 'palie, -la+ \n [NL, fir. poly-+ my-ositis]: in-flammation of several muscles at once

MYODIAN

Poly-myositis \;pilē, -la+\ n [NL, fr. poly- + myositis]; inflammation of several muscles at once
polym.y-thy \ pol'imothe: \;pale.mithē, \ -la.m.\ n \ -es [NL
polymythia, fr. Gk polymythia with many legends (fr. poly- +
mythos myth) + NL \ -la \ -y \ -more at MYTH]; the inclusion

of the mythos myth) + NL \ -la \ -y \ -more at MYTH]; the miclusion

of the mythos myth) + NL \ -la \ -y \ -more at MYTH]; the miclusion

of the mythos mythology of the my

polymythia, fr. Gik polymythos with many legends (fr. poly-polymythia, fr. Gik polymythos of many or several stories or plots in one narrative or dramatic work poly-myxa (specific epithet of Bacillus polymyxa — fr. poly-myxa (specific epithet of Bacillus polymyxa — fr. poly-myxa (specific epithet of Bacillus polymyxa — fr. poly-myxa — h. FlSV·in]: any of several basic polypeptide toxic antibiotics that are obtained from strains of a soil bacterium (Bacillus polymyxa) and are active against gram-negative bacteria: as a or polymyxin B: the least toxic of the polymyxin sued in the form of its sulfate chiefly in the treatment of some localized, gastrointestinal, or systemic infections poly-new (**p-na*) n-s[Sw]: a tart made of rich cookie dough, filled with meringue to which ground almonds have been added, and topped with a cross made of two strips of the cookie dough, and the summer of some localized, gastrointestinal, or systemic infections poly-nemid \phipilenemid, nem-\na* fill Polynemidae]: a fish of the family Polynemidae
poly-nemid \phipilenemid, nem-\na* n-s [NL Polynemidae]: a fish of the family Polynemidae
polynemid-dae \na* -nem-\na* of file dishes that resemble mullets but have the pectoral fin divided into two parts of which the upper is much like an ordinary fin and the lower is composed of several separate slender threadlike rays and abound on the sandy shores of warm seas, many of them being valued for food and some yielding isinglass
poly-ne-mold \na* n-s: a polynemidae
polynemida* or related to the Polynemidae
polynemid \na* n-s: a polynemidae
polynemid \na* n-s: a polynemidae
polynemid \na* n-s: a sense fine divided into two parts of home and the sense of the family Polynemidae
polynemidae; a suborder of Percomorphi coextensive with the family Polynemidae of fishes resembling mullets
family Polynemidae; of fishes resembling mullets
family Polynemidae; of fishes resembling mullets of the family Polynemidae; of fishes resembling mullets of the family Polynemidae; of fishes resembling mullets of the

tall stature, and large-boned build 2: a group of Austronesian languages spoken largely in Polynesia polynesian chestnut n, usu cap P 1: a Polynesian tree (Inocarpus edulis) of the family Leguminosae 2: the edible kidney-shaped seed of the Polynesian chestnut polyneuritic \pini_sil-sil-sil-ned (INL polyneuritis + B-lc]: of, relating to, or marked by polyneuritis + B-lc]: of, relating to, or marked by polyneuritis in euritis of several peripheral nerves at the same time caused by alcoholism, metallic and other poisons, infectious disease, or vitamin deficiency (as of thiamine) poly-neuropathy \(^3+\) \(^1+\) \(^1\) \(^1\) \(^1+\) \(^1+\) \(^1\) \(^1+\) \(

worm.

Worm.

Worm.

Worm.

Deli'noid.ae \,pile'noid.)dē, pp.line'wī(.)dē\ n pl. cap [NL. fr. Polynoe, type genus (fr. Ck Polynoe, a sea nymph) + -ldae]: a family of marine polychaete worms having the back covered with two rows of scales in binomial \,'pile'nomes, \, |si_n\\ n = [poly- + -nomial \, ipile'nomes, \, |si_n\\ n = [poly- + -nomial \, (as in binomial)] 1 a: a mathematical expression of two or more terms b: an algebraic function of one or more variables consisting of the sum of terms whose factors are constants or positive integral or zero powers of the variables — called also integral rational junction 2: a technical name of a plant or animal consisting of a descriptive phrase of more than three words

animal consisting of a descriptive phrase of more than three words

2polynomial \"\ adj 1: having the character of a polynomial

2: consisting of many names or terms

poly-nuclear \[\text{palle}, \] -la+\\ adj \[\text{ISV poly-} + nuclear \] : containing more than one nucleus: a: POLYNCICLE a b: containing more than one central atom or ion—used of coordination complexes o: POLYMORPHONUCLEAR

poly-nucleo-sis \[\text{-serve}, \text{if}, \] is polynucleo-ses

\[\frac{-0.62}{-0.62} \] \[\text{INL}, \] fr. \[\text{ISV polynucle-} \] in polynucleo-ses

\[\frac{-0.62}{-0.62} \] \[\text{INL}, \] fr. \[\text{ISV polynucle-} \] in polynucleory + \[\text{NL} \]

\[\frac{-0.62}{-0.62} \] \[\text{INL}, \] fr. \[\text{ISV polynucle-} \] in polynucleotide \[\text{palle}, \] -la+\\ n \[\text{ISV polyn-y-} + nucleotide \] : a nucleotide \[\text{as in the circulating blood} \]

\[\text{poly-nya also po-lyn-ia} \] \[\text{pallon-lys} \] n-s \[\text{Russ polyn-ya, fr. poly- poly, note, also note also note at \[\text{Floor} \]

\[\text{poly-open, hollow; akin to OSlav polye field — more at \[\text{Floor} \]

\[\text{Poly-open, hollow; akin to OSlav polye field — more at \[\text{Floor} \]

\[\text{Poly-open, hollow; akin to OSlav polye field — more at \[\text{Floor} \]

\[\text{Poly-open, hollow; akin to OSlav polye field — more at \[\text{Floor} \]

\[\text{Poly-open, hollow; akin to OSlav polye field — more at \[\text{Floor} \]

\[\text{Polye open, hollow; akin to OSlav polye field — more at \[\text{Floor} \]

\[\text{Polye open hollow; akin to OSlav polye field — more at \[\text{Floor} \]

\[\text{Polye open hollow; akin to OSlav polye field — more at \[\text{Floor} \]

\[\text{Polye open hollow; akin to OSlav polye field — more at \[\text{Floor} \]

\[\text{Polye open hollow; akin to OSlav polye field — more at \[\text{Floor} \]

\[\text{Floor} \]

\[\text{Floor} \]

**taining many double bonds 2: a polymer of olefin (as polycthylene)

**poly-0n-y-mous \phile inames\ ad I [Gk polyönymos, fr.
poly-0n-y-mous \phile inames\ ad I [Gk polyönymos, fr.
poly-0n-y-my _ne_inames\ n= s [Gk polyönymda, fr. poly-0nymia (fr. onoma name + ia sy)]: plurality of names: the
use of various names for one thing
poly-ong \phile inames\ n= s [NL, fr. poly- +-opla]: perception
of more than one image of a single object esp. with one eye
: multiple vision: ppr_opla — poly-opic _n=iplik\ adj
poly-or-childism _n=iplic | fr. poly- +-opla]: S \\
poly-or-childism _n=iplic | fr. poly- +-opla]: having many
organic \\
poly-organic \\
politim i a condition of having more than two testes
poly-organic \\
politim i a condition of having more than two testes
\text{adj foly-} + organic]: having many
organic \\
\text{adj foly-} + organic]: having many
\text{adj foly-} + organic]: having many
\text{adj foly-} + organic]: having many

organs
poly-os-tot-ic \\\partial_{poly-} + organic]: having many
poly-os-tot-ic \\\partial_{poly-} + ost + ostc]
: involving or relating to many bones
poly-ovular \\\partial_{poly-} + ost + ostc]
poly-ovular \\\\partial_{poly-} + ost - ostc]

containing more than one ovum \(\simeq \text{cycle}\) \(\simeq \text{collicle}\)

poly-ovullar \| ipilië+\| adj [poly- + ovular] \| : of, relating to, producing, or containing more than one ovum \(< \infty \corr \) cycle\| \(< \corr \) (corr \)

COUS

pol-yp-ary \päla,per\ n -ES [polyp + -ary]: the common investing structure or tissue in which the polyps of corals and other compound forms are embedded pol-yp-ean *-sp*en\ ad [polyp + -an]: relating to or like a

polypean \(\text{"spean} \) \(ad \) \(polyp + -ad \) \(restains to o \) \(ad \) \(polyp + -at \) \(restains to o \) \(ad \) \(polyp + -at \) \(restains to o \) \(ad \) \(polyp + -at \) \(polyp + -ad \) \(polyped \)

processes

1001y-pe-datid \:----datd-dd-dd-dd-dd-lNL Polypedatidae]

101 of or relating to the Polypedidae

2001ypedatid \"\"\" s: a aree from of the family Polymetadid